Genome Editing of Sinusoidal Endothelial Stem Cells for Permanent Correction of Hemophilia A

Grant Award Details

Genome Editing of Sinusoidal Endothelial Stem Cells for Permanent Correction of Hemophilia A

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10524

Investigator:

Name:	Saswati Chatterjee
Institution:	City of Hope, Beckman Research Institute
Type:	PI

Disease Focus: Blood Disorders

Award Value: $2,182,193

Status: Pre-Active

Grant Application Details

Application Title: Genome Editing of Sinusoidal Endothelial Stem Cells for Permanent Correction of Hemophilia A

Public Abstract:

Research Objective

Therapeutic candidate to cure hemophilia A is AAV-based genome editing vector that corrects the disease-causing mutation in the factor VIII gene in patient stem cells to develop a permanent cure.

Impact

Permanent correction of hemophilia A by editing mutations in the FVIII gene in stem cells. Develop a precise and efficient non-nuclease genome editing technology for editing somatic stem cells in vivo.

Major Proposed Activities

- Identification of optimal genome editing vector for editing the FVIII gene in human endothelial cells, somatic stem cells and immortalized cells derived from hemophilia A patient.
- Test successful in vitro genome editing in the human stem cells that give rise to the clotting factor VIII producing cells.
- Demonstrate genome editing of the FVIII gene in human stem cells and their progeny, to provide proof of concept of the gene editing strategy for therapeutic correction of the mutation.
- To identify the best genome editing vector for correcting xenotransplanted human stem cells in immune-deficient mice in vivo.
- Functional evidence of genome editing of FVIII gene in regenerating mouse liver after partial hepatectomy.
- Test therapeutic correction of hemophilia A in a dog model to obtain proof of efficacy of this genome editing strategy. This information will facilitate translation and discussions with the FDA.

Statement of Benefit to California:

Hemophilia A is an incurable, devastating inherited bleeding disorder caused by the lack of functional clotting factor Vlll. The management of hemophilia A poses a large economic and quality of life burden. Twenty percent of all hemophilia patients live in California. We plan to develop a therapeutic candidate for the correction of the causative factor VIII mutations in stem cells using genome editing in order to develop a permanent cure for hemophilia A.
